AD-A188 276 ATROPINE STRESS AND HUMAN PERFORMANCE(U) OKLAHOMA UNIV HEALTH SCIENCES CENTER OKLAHOMA CITY H L WILLIAMS 31 OCT 85 DAMD17-83-C-3194 1/1

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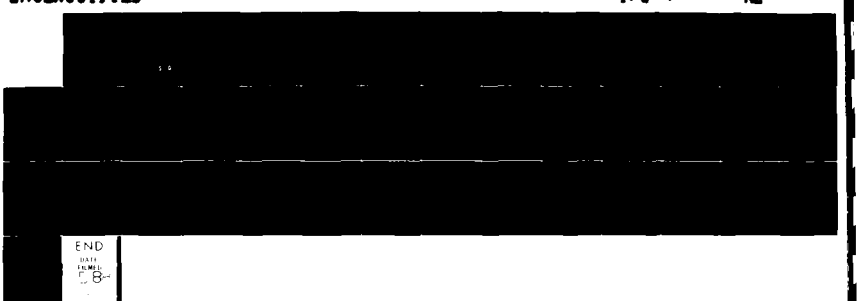

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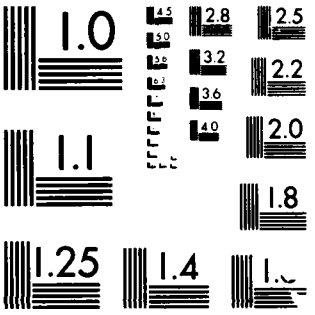

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CONTRACT NO. DAMD17-83-C-3194

TITLE: Atropine, Stress, and Human Performance

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REPORT DATE: October 31, 1985

TYPE OF REPORT: Annual

PREPARED FOR: U.S. ARMY MEDICAL RESEARCH & DEVELOPMENT COMMAND
Fort Detrick, Frederick, Maryland 21701-5012

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

Form Approved OMB No. 0704-0188

1a. REPORT SECURITY CLASSIFICATION: Unclassified	1b. RESTRICTIVE MARKINGS
2a. SECURITY CLASSIFICATION AUTHORITY	3. DISTRIBUTION/AVAILABILITY OF REPORT: Approved for public release; distribution unlimited
2b. DECLASSIFICATION/DOWNGRADING SCHEDULE	
4. PERFORMING ORGANIZATION REPORT NUMBER(S)	5. MONITORING ORGANIZATION REPORT NUMBER(S)
6a. NAME OF PERFORMING ORGANIZATION: University of Oklahoma Health Sciences Center; 6b. OFFICE SYMBOL (If applicable)	7a. NAME OF MONITORING ORGANIZATION
6c. ADDRESS (City, State, and ZIP Code): P.O. Box 26901, Oklahoma City, Oklahoma 73190	7b. ADDRESS (City, State, and ZIP Code)
8a. NAME OF FUNDING/SPONSORING ORGANIZATION: U.S. Army Medical Research & Development Command; 8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER: Contract No. DAMD17-83-C-3194
8c. ADDRESS (City, State, and ZIP Code): Fort Detrick, Frederick, Maryland 21701-5012	10. SOURCE OF FUNDING NUMBERS

PROGRAM ELEMENT NO.	PROJECT NO.	TASK NO.	WORK UNIT ACCESSION NO.
63764A	3M46-3764D995	AA	012

11. TITLE (Include Security Classification): Atropine, Stress, and Human Performance

12. PERSONAL AUTHOR(S): Harold L. Williams, Ph.D.

13a. TYPE OF REPORT	13b. TIME COVERED	14. DATE OF REPORT (Year, Month, Day)	15. PAGE COUNT
Annual	FROM 9/30/84 TO 9/29/85	1985 October 31	

16. SUPPLEMENTARY NOTATION

17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
FIELD	GROUP	SUB-GROUP	
06	15		
06	19		

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT	21. ABSTRACT SECURITY CLASSIFICATION
☐ UNCLASSIFIED/UNLIMITED ☐ SAME AS RPT. ☐ DTIC USERS	

22a. NAME OF RESPONSIBLE INDIVIDUAL	22b. TELEPHONE (Include Area Code)	22c. OFFICE SYMBOL
Mrs. Virginia M. Miller	301/663-7325	SGRD-RMI-S

DD Form 1473, JUN 86 — Previous editions are obsolete. — SECURITY CLASSIFICATION OF THIS PAGE

FOREWORD

"In the conduct of research where humans are the subjects, the investigator(s) adhered to the policies regarding the protection of human subjects as prescribed by 45 CFR 46 (Protection of Human Subject)."

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1. Statement of the Problem

The major aims of this research program are to investigate dose effects of atropine combined with such stress-related variables as sleep deprivation and/or moderate pre-dose exercise on cognitive performance and psychophysiology of healthy young men. Employing an integrated between-and within-subjects repeated measures design, the major aim of the second year of work was to investigate the independent and combined effects of a single intramuscular, 2 mg dose of atropine and one night of sleep deprivation on a battery of selected physiological variables, self-ratings, and cognitive tasks designed to be sensitive to each of the two treatments. The cognitive tasks have face validity for certain information-processing jobs likely to be encountered in contemporary military work.

The effects of atropine on most of the physiological variables selected for this research are well documented but we found no studies of atropine effects in combination with sleep deprivation.

2. Rationale

From the perspective of military requirements, the research literature suggests that a relatively small, i.m. dose of atropine (e.g., 2 mg) can impair cognitive functions that are essential components of a number of field jobs (e.g., Headley, 1982). Sleep deprivation also causes impairment on tasks that have military relevance (e.g., Wilkinson, 1969; Frowein, 1981; Sanders, Wijhen and V. Arkel, 1982). However, we do not know whether these two treatments have additive or hyperadditive (interactive) effects on performance.

3. Background and Literature Review

a. Effects of atropine on information processing

Most studies of the effects of cholinergic drugs (and of sleep deprivation) on psychomotor functions have been task-focused and empirical. Typically, such research employs a broad-ranging battery of performance tasks, each of which challenges a variety of skills. Although the profiles of task scores may differ systematically for different treatments (e.g., different drugs), precise conclusions about which cognitive functions are differentially affected by a given treatment are difficult to make. The tasks used in such studies usually lack theoretical underpinnings and the skill components represented in the tasks are often too complexly organized for valid functional analysis.

For the first year of the contract, the present research was also primarily empirical and task oriented. However, the findings from that year, considered with some relatively recent results and concepts from other investigators led to hypotheses about specific functional impairments likely to be observed both for atropine effects and sleep deprivation. These ideas stem from recent attempts to integrate concepts and data from contemporary

cognitive psychology to data on the effects of cholinergic drugs and of sleep loss on information processing. Thus, for cholinergic compounds, Warburton in his 1977 review concluded that the ascending cholinergic reticular pathways mediate the recognition and selection of environmental stimuli, while having little involvement in the selection and organization of responses. Evidence for these notions came first from animal studies in which cholinergic agonists such as physostigmine improved signal detection performance (Warburton & Brown, 1972) while cholinolytics, such as scopolamine, disrupted signal-detection performance (Brown & Warburton, 1971). Analysis of their data, employing signal detection statistics, showed that scopolamine-induced changes in signal-detection performance resulted from impaired perceptual sensitivity (d') rather than altered response criteria (β). Warburton and his colleagues concluded that central cholinergic blockade disrupts vigilance performance by causing specific impairment of perceptual sensitivity. Later, Wesnes and Warburton (1984) showed that 2 compounds, scopolamine and nicotine, which have opposite effects on central cholinergic pathways, produce opposite effects on visual signal detection in a high-speed visual information-processing task. Calloway (1984) employed a serial-stage information-processing theoretical model of choice reaction-time and Sternberg's (1969) additive-factor method to examine the effects of several psychotropic chemicals on human performance. Using information-processing tasks in parallel with event-related brain potentials, Calloway also concluded that scopolamine differentially impairs perceptual processes associated with the analysis and encoding of visual information but that it does not impair certain output processes such as those associated with response selection and organization. More attention will be given to serial stage processing models later in this report.

The dichotomy between input (perceptual) and output (response) processing suggested by these investigators matches the functional distinction between cholinergic and aminergic neurochemical systems suggested by others. For example, Vanderwolf and Robinson (1981) proposed that there are two kinds of input from the reticular activating system to the hippocampus and cortex, cholinergic and aminergic. They suggest further that the cholinergic system may have an important role in the mediation of signal identification whereas the aminergic system may mediate motor preparation and control.

During our first year of work on this project, some of our tasks placed relatively greater load on perceptual functions such as signal encoding whereas others put greater load on output functions such as response preparation and motor control. As could have been predicted from the research cited above, we found that the tasks which were most sensitive to dose effects (up to 2.0 mg) of atropine were those that loaded perceptual functions such as signal recognition. One such task required aircraft detection. The subject was taught to discriminate two aircraft silhouettes, differing slightly in shape. One silhouette was designated "friendly," the other "enemy." Failure to "detect and destroy" the enemy target within 700 ms of target onset resulted in an aversive white flash. False alarms (shooting down friendly aircraft) resulted in a rather unpleasant buzz. Bonus points, convertible to cash, accrued for fast and accurate responses. Statistical analyses revealed a systematic dose effect of atropine on the signal detection statistic d'

but no drug effect on the so-called "caution" statistic, β. The monotonic decrease in d' with atropine dose was due both to a decrease in "hits" on enemy targets and an increase in "false alarms." We concurred with Warburton and colleagues that atropine impaired signal detection by decreasing perceptual sensitivity (d') and not by altering response decision criteria (β). Reaction time in the aircraft detection task was not affected by atropine, probably because of the deadline procedure employed to control response speed.

Given the results summarized above, we expected to find systematic atropine effects on a three-dial oddity matching task, either on accuracy or speed. For our well-practiced subjects, accuracy on this task was very high, averaging better than 90% in nearly all conditions, indicating that the oddity matching task as designed was probably too easy. Statistical analysis revealed a just significant ($p < .04$) effect of atropine on accuracy and no effect of the drug on reaction time. We had again used a deadline procedure to control performance speed.

In year one, we also employed a 2-dimensional compensatory tracking task in which the subject, manipulating a joystick, attempted to hold a cursor within a stationary annulus and cross-hair. The cursor was computer-driven by a sum of X-Y inputs derived from a complex Lissajous function. Although overall accuracy was also quite high on this task, tracking error increased as a monotonic function of atropine dose.

Atropine alone had no systematic effect on another task, interval estimation. However, when pre-dose exercise was added to the protocol, errors in interval estimation increased systematically with atropine dose. For nearly all subjects, the interval-estimation task has an important motor component because most subjects try to maintain accurate estimation accuracy by rhythmic movements of the hands or feet. As summarized earlier, the results of recent studies suggest that with relatively small doses, muscarinic blockers may not impair motor output functions. However, pre-dose exercise appears to have increased the potency of atropine for influencing motor output.

Atropine had no effect on mental arithmetic accuracy, a task designed to load working memory. Furthermore, no atropine dose effects were found after the introduction of pre-dose exercise on this task. For information processing, our results in the first year with atropine alone were generally consistent with the hypothesis put forth by Wesnes and Warburton (1984) and by Calloway (1984) that antimuscarinic agents cause selective impairment of input perceptual functions like signal recognition and analysis rather than of output motor functions like response selection and organization.

b. Atropine effects on physiological variables.

As expected from the work of many others, heart rate was extremely sensitive to atropine, increasing as a function of dose. Pupil diameter also increased with atropine but only at the 2 mg dose. Skin conductance decreased with dose. Pre-dose exercise appeared to enhance the potency of atropine for affecting autonomic activity. For example, pupil dilation was now found with a 1 mg dose. In general, these physiological data indicated that we were

obtaining dose-related pharmacological effects of atropine, all of which were observed in 30-60 minutes post dose. However, we will report later that there is a considerable lag between these autonomic effects and the development of centrally mediated cognitive deficits.

c. Self-Reports

As atropine dose increased in our Year 1 studies, subjects reported feeling more sleepy and weary. They felt that they were less efficient, more confused, slower and less steady. Some of them also reported blurred vision and a sense of dryness. These findings are consistent with self-assessment data reported by several other investigators. As will be discussed later, for Year 2 we introduced the multiple sleep latency test which is a direct measure of sleep tendency (i.e., sleepiness). We intend to compare the self reports and the sleep latency measures with one another.

d. Effects of sleep deprivation on information processing

There is evidence that sleep deprivation, like atropine, also has selective effects on information processing. Employing a serial stage theoretical model of information processing, Frowein et al. (1981) and Sanders et al. (1982) found that the variable, sleep state (normal or sleep-deprived) interacted specifically with the effects of two task-related experimental variables, signal quality and time uncertainty, on choice reaction time. The effects of two other task-related variables, signal intensity and stimulus-response compatibility were found to be additive to those of sleep state. The effects of the task variables among themselves were generally additive.

Where such additivity exists among certain task-related variables, serial stage theorists infer that each task variable influences selectively a different stage in the reaction process. Thus, signal intensity, signal quality, stimulus-response compatibility and time uncertainty are said to influence a stimulus preprocessing stage, a stimulus identification stage, response selection and response preparation stages, respectively. If a new experimental variable such as sleep loss or a drug is found to interact specifically with one or more task variables but to have additive effects with others, the usual interpretation is that the new variable and the task variable with which it interacts each influence the same hypothetical stage in the reaction process. The results summarized earlier suggest that sleep deprivation slows processing selectively at two stages in the reaction process, signal identification and response preparation.

These hypotheses and findings led to some rather specific predictions about likely performance deficits during the second year of this contract, as follows:

d.1 Like atropine, sleep deprivation should impair performance on the aircraft signal detection task and the effects of the two treatments on the signal detection statistic, d', should be interactive rather than additive.

d.2 In a choice reaction-time task, both sleep loss and atropine effects should interact with those of the task variable, stimulus quality. Neither treatment should interact with the task variable, stimulus response compatibility, but sleep loss effects alone should interact with those of time uncertainty. Because both sleep loss and atropine cause specific slowing in a signal analysis/recognition stage, the two treatments combined should have interactive effects on reaction time.

d.3 If the two treatments, sleep loss and atropine, have interactive effects on choice reaction time and if each treatment interacts with the effects of stimulus quality, then we will conclude that both treatments influence a signal identification stage of information processing. They may not, however, influence the same functions within that stage. For that reason it will be interesting to learn whether a significant 3-way interaction exists between the effects of atropine, sleep loss and the task variable, stimulus quality.

d.4 The effects of the two treatments, atropine and sleep loss, should also interact on d' in the auditory signal detection task. However, previous research by ourselves and others indicates that atropine should not affect the so-called "caution" statistic β. Whether sleep deprivation will affect this index of a hypothesized decision strategy remains to be seen.

4. Experimental Methods for Year 2.

a. Subjects

Thirty-two men in excellent health ranging in age from 19 to 44 volunteered and were accepted into the study. Volunteers were recruited both by posters placed on college bulletin boards in the Oklahoma City area and from local employment placement agencies. Before acceptance into the study, each volunteer was screened for physical and mental health, medical history and current drug or medication usage. Although no urine tests were ever administered, each volunteer was asked if he would be willing to undergo urinalysis to verify that he was drug free. If his answer was "No", he was not invited to enter the project.

After reading and signing a consent form approved by our Institutional Review Board, the volunteer received a standard physical examination conducted by our physician, Timothy Hill, and an exercise stress test in the laboratory of Dr. Carl Rubenstein. If the volunteer passed those tests he was scheduled for a series of practice sessions on the performance battery and for the experimental sessions involving i.m. atropine (2 mg) or placebo, with or without sleep deprivation. Volunteers were scheduled in pairs and one member of each pair was randomly selected for the atropine condition, the other for placebo. The experiments were run single blind. A volunteer was guaranteed a base pay of $50/day for each complete experimental day and could earn up to $50.00 per experimental day in bonus points for good performance. Practice sessions were not financially compensated.

b. Research Environment

The study was conducted at the Oklahoma Center for Alcohol and Drug-Related Studies which is a research unit of the Department of Psychiatry and Behavioral Sciences of the University of Oklahoma College of Medicine. The Center occupies approximately 3,000 sq. ft. of space on the 4th floor of the Rogers Building located at 800 NE 15th St., Oklahoma City, OK, 73104. The research staff consisted of Harold L. Williams, Ph.D., Center Scientific Director, his co-principal investigators, Frank Holloway, Ph.D. and John Carney, Ph.D. (Pharmacology) and the technical staff, Garnet McLean, M.S., Laboratory Manager, L. T. Smith, M.S., Systems Programmer, Kimberly Treas, Research Assistant, and Clay Reaves, Research Technician; Timothy Hill, M.D., Ph.D., and Carl Rubenstein, M.D., served as consultants for the project.

c. The Test Battery

There were 3 subtests in the battery but because of time constraints they were run 2 at a time. The tests were (1) Aircraft Visual Signal Detection, (2) Oddity Matching and (3) Auditory Signal Detection.

c.1 Aircraft Signal Detection

On task initiation, 100 randomly located points on the screen of the Intecolor 800/Graphics computer are presented in red on a black background. The subject is instructed that these points represent both friendly and enemy aircraft flying at the perimeter of his video detection system. During the 15-minute task period, a randomly varying number (20 to 30) of these points, selected at random, are relocated to new randomly selected points on the screen. At random intervals, from to 2 to 5 seconds, a red aircraft silhouette is presented head-on. The silhouette appears to emerge gradually from an enlarging, randomly selected point on the screen. The enlarging point, taking on the shape of an aircraft silhouette, appears to be an approaching plane. However, whether it is friend or foe cannot yet be determined. This event may be a "feint," in which case the aircraft appears to approach, but when its wing span reaches 1/2 inch, it turns to one side or the other and retreats into the background noise. This aborted approach requires 300 milliseconds and the silhouette remains ambiguous as to type throughout. These feints are intended as catch trials and we record erroneous anticipatory responses. If the trial is a complete approach, the silhouette continues to approach for an additional 225 milliseconds, growing to a 1-inch wingspan. These displays have visible features which distinguish them as "Friend" or "Foe."

If the silhouette is a foe, the subject is to press a "Fire" button within 700 milliseconds of silhouette onset. If he succeeds, the target explodes in yellow and a correct detection (Hit) is recorded. If he fails to fire within the 700 millisecond deadline, the foe "fires" at him, i.e., the screen flashes white for 250 milliseconds, and an error of omission is recorded. If the silhouette is a friend, the subject is to withhold fire. If he does so, the friend will turn away. A correctly withheld response is then recorded. If he fails to hold fire, the friendly target explodes in blue

and an error or commission (False Alarm) is recorded.

The ratio of feints to complete approaches is 2:1 and the probability of friend is 0.5. The dependent variables are the signal detection statistics, d' and β, percent Hits and percent False Alarms the number of anticipatory errors and reaction time.

At the beginning of the year, we recorded EEG during this task but found that eye movement and other artifacts were too numerous for valid recording.

c.2 Auditory Vigilance

With eyes closed, the subject hears a randomly ordered series of tone pings composed of 5 different pitches (850, 1000, 1150, 1300 and 1800 Hz), the lowest of which is the target ping. The subject is to press a button as quickly as possible to the target ping. The interstimulus interval for the nontarget ping is 2 seconds. When the target ping occurs, the subsequent ping follows the subject's response by 2 seconds. The deadline for responding is 1 second. There are 48 randomly occurring target pings per 7.5 minute block and there are 4 blocks per session. Thus, the task lasts for about 30 minutes. The response variables are d', β, Hits, False Alarms and reaction time. EEG is recorded throughout the task and will be analyzed off line in a search for EEG predictors of performance breakdown.

c.3 Oddity Matching

This task and task-related experimental variables are designed to test hypotheses about the specific effects of atropine and sleep loss on stages in a serial stage theoretical model of information processing. The subject is presented with a series of displays composed of 4 dials arranged in a square. Each dial contains a pointer, one of which points in a different direction than the other three. The subject is to identify the odd pointer, lift his finger from a center button (reaction time) and move it one centimeter to press the designated one of 4 buttons also arranged in a square as fast as he can (motor time). There are 3 orthogonally programmed task variables, each targeted upon a different hypothetical stage in the reaction process. These are Display Quality (to influence target identification), Stimulus-Response Compatibility (to influence response selection), and Time Uncertainty (to influence response preparation). Low display quality is produced on half the trials by superimposing a random-dot mask over the screen. Low stimulus-response compatibility (SRC) is produced on half the trials by altering the rule for mapping of the motor response on the stimulus. In the low SRC condition, the subject is to respond on the button located one step clockwise from the spatial location of the stimulus. Low time certainty is produced on half the trial blocks by varying the interstimulus interval from 1 to 3 seconds. This task is experimenter-paced but does not employ a deadline procedure. There are 4 blocks of trials (2 with regular, 2 with variable ISIs) and the total time on task is about 18 minutes.

The Compensatory Tracking/Interval Estimation Task planned for the second year was dropped because of time constraints.

d. The physiological measures

These measures include heart rate, systolic,diastolic and mean blood pressure, pupillary diameter measured from photographs of the light-adapted eye, multiple sleep-latency tests and the electroencephalogram. The cardiovascular measures were taken before and after each performance cycle. Photographs of the eye were taken at the end of each performance cycle.

Sleep latency was assessed 3 times a day, following each performance cycle. Sleep onset was defined as the appearance of one uninterrupted minute of EEG Stage 1 (Rechtschaffen and Kales, 1968). Stage 1 onset was defined by recordings from scalp locations Oz and Cz referred to the linked earlobes. For subjects with little or no waking alpha rhythm, the electrooculogram was also recorded in order to observe the slow eye movements usually found at Stage 1 onset. The tape recorded electroencephalogram, recorded continuously during the auditory vigilance task, was taken from three scalp derivations, Oz, Pz and Cz. The recordings will be analyzed off line for possible EEG predictors of upcoming processing errors.

e. Self Ratings

Before and after each of the three task cycles, the subject assessed his state on a set of 40 items, 29 of which were bipolar adjectives like DROWSY-ALERT. The item list is the same as that used in Year 1 of this contract.

f. Overall Design

The second-year plan called for investigation of the independent and combined effects of a single dose of atropine (2 mg) and a night of sleep deprivation on performance. The design was an integrated between-subjects (Drug), within subjects protocol in which 2 volunteers participated each week. One volunteer was randomly selected for the atropine doses, the other for placebo. The experiment was run single blind.

f.1 The research design is an ABCA where A = baseline, B = atropine sulphate (2 mg) or normal saline administered i.m. in the thigh, and C = atropine plus one night of sleep deprivation. The order of treatments B and C was counterbalanced across subjects. Typically, a pair of volunteers reported to the laboratory Tuesday evening at 1900 for practice on the performance tasks. They practiced two full task cycles on Wednesday and slept in the laboratory Wednesday night. Thursday was baseline day A1. Depending on the counterbalanced design, the subjects were either sleep deprived or not on Thursday night, remaining all night in the laboratory in either case. Again, depending on counterbalancing, Friday was either B (drug alone) or C (drug + sleep loss). The two volunteers were escorted home Friday afternoon and were off until Sunday evening. They were either sleep deprived or not Sunday night so that Monday was either session B or C. They slept in the laboratory Monday night and Tuesday was the final baseline session, A2.

f.2 Session Schedule

For a full laboratory session, the schedule of events was typically as follows:

0630 hrs.	Wake up
0700	Breakfast
0730	Physiological recording harness attached
0800	Physiological recording (heart rate, blood pressure and Mood Assessment)
0810	Performance Test Cycle #1. Aircraft Signal Detection, Auditory Vigilance, Oddity Matching (counterbalanced order)
0940	Photograph of the eye, Sleep Latency Test
1000	Physiological recording and Mood Assessment
1010	Recess while other subject ran
1130	Atropine or placebo injection
1200	Physiological recording, photograph of the eye and Mood Assessment
1210	Test Cycle #2
1340	Photograph of the eye, Sleep Latency Test
1400	Physiological recording and Mood Assessment
1410	Lunch Break
1545	Physiological recording and Mood Assessment
1555	Test Cycle #3
1725	Photograph of the eye, Sleep Latency Test
1745	Physiological recording and Mood Assessment

5. Results

A. Performance Tasks

A.1 Aircraft Signal Detection

A.1.a Effects of Sleep Deprivation

Table 1 displays means and standard deviations for the aircraft signal detection task. Note that the columns represent days within drug groups and the major rows cycles within days. For convenience, days A1, B, C, and A2 are numbered 1, 2, 3 and 4. For the hypotheses that both atropine and sleep-deprivation should impair perceptual sensitivity, the response variable of greatest interest is the signal detection statistic d'. Recall that cycle 1 testing occurred prior to injection of drug or placebo, and that on day C (labeled 3 in Table 1), cycle 1 testing followed a night of sleep deprivation. As can be seen in Table 1, the average d' score in cycle 1 decreased on day 3 in both the atropine and placebo group. Note also the decrease in Hits, the increase in False Alarms and the absence of a systematic effect of sleep loss on β or reaction time. These trends are generally as predicted for this task. To test for significant sleep loss effects, we computed the difference score $\frac{\text{Day 4} + \text{Day 2}}{2}$ - Day 3 on each response variable for each subject, on cycle 1 scores only, and tested the mean difference score with t_o for

TABLE 1

AIRCRAFT DETECTION TASK

GROUP

ATROPINE (N = 16)

DAYS

Cycle		1 $\bar{X}$	1 S	2 $\bar{X}$	2 S	3 $\bar{X}$	3 S	4 $\bar{X}$	4 S
1	d'	5.1	3.2	5.6	3.1	3.8	2.2	6.5	2.9
	H	92.9	8.7	95.9	4.6	86.6	18.3	97.4	6.2
	FA	6.8	11.6	4.7	9.6	8.4	9.5	5.1	4.3
	ß	1.4	1.3	1.9	1.6	1.8	1.7	0.8	0.5
	RT	687	89	689	79	685	79	658	86
2	d'	5.3	2.9	5.2	2.5	2.7	1.6	6.1	2.8
	H	94.5	8.5	88.4	24.2	80.8	20.0	97.3	4.8
	FA	8.8	14.8	5.5	8.0	10.7	12.7	4.3	6.4
	ß	0.9	1.2	2.1	2.1	1.7	1.0	1.2	1.6
	RT	675	66	670	88	670	88	654	88
3	d'	4.3	2.7	3.2	1.3	1.9	1.0	6.2	3.0
	H	94.3	6.3	91.8	8.3	75.6	15.8	96.9	6.3
	FA	8.4	10.1	9.1	9.1	16.5	14.1	5.7	11.0
	ß	1.2	1.3	2.0	0.9	1.5	0.6	0.9	1.2
	RT	680	83	675	84	688	82	641	98

PLACEBO (N = 16)

DAYS

Cycle		1 $\bar{X}$	1 S	2 $\bar{X}$	2 S	3 $\bar{X}$	3 S	4 $\bar{X}$	4 S
1	d'	5.8	2.5	5.9	2.7	3.8	1.8	5.6	2.4
	H	95.2	5.6	97.3	4.1	89.6	6.3	97.6	2.4
	FA	8.1	7.5	4.3	5.4	7.0	7.5	3.8	4.7
	ß	1.0	1.7	0.7	0.6	1.3	1.9	1.4	1.6
	RT	652	84	646	66	650	67	628	66
2	d'	4.8	2.7	6.2	2.6	4.9	3.2	5.4	2.8
	H	94.2	7.0	96.7	6.0	93.5	7.2	96.9	3.6
	FA	6.0	7.1	4.4	6.2	6.4	5.9	5.3	6.4
	ß	1.1	1.2	1.5	1.8	1.2	0.8	1.3	1.5
	RT	667	71	630	73	659	80	625	72
3	d'	4.1	1.9	5.7	2.6	3.7	2.4	6.3	2.5
	H	94.2	7.8	94.6	7.1	88.1	12.3	97.7	3.7
	FA	7.9	7.8	5.0	7.0	8.1	8.7	4.0	4.6
	ß	1.2	1.6	2.2	2.2	2.0	1.8	1.1	1.6
	RT	671	73	631	72	668	69	618	69

Legend

DAYS: 1 = Baseline, 2 = Atropine or Placebo, 3 = Atropine or Placebo plus Sleep Deprivation, 4 = Baseline

Response Variables: H = Percent Hits, FA = Percent False Alarms, RT = Choice Reaction Time

correlated means. As predicted, the effect of sleep deprivation on d' was significant (t_o = 5.6, df = 31, p <.001) as were also the effects on Hits (t = 3.7, p <.001) and False Alarms (t = -3.8, p <.001). Figure 1 illustrates the effect of sleep deprivation on d'. The mean difference score for β was also statistically significant but perusal of the means in Table 1 reveals that this apparent sleep loss effect is spurious. Note, for example, that in the atropine group, β showed a large drop from average daily values on day 4 (final baseline) and that in the placebo group, there was a large drop on day 2. In neither group was there any marked change during sleep deprivation (day 3). As expected with the deadline procedure employed here, sleep loss had no significant effect on average reaction time in cycle 1.

A.1.b Atropine Effects on Performance

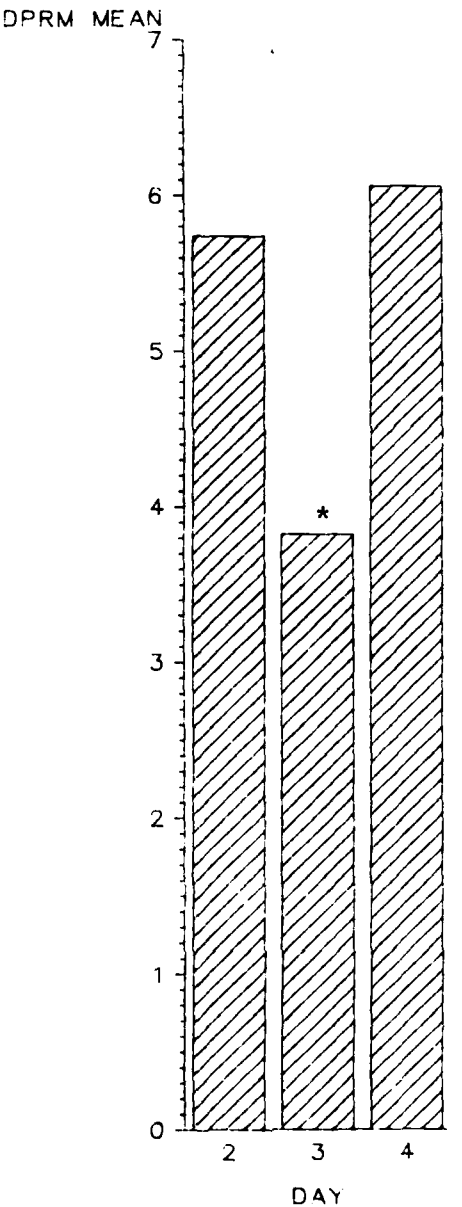
Atropine (2 mg) or placebo (normal saline) were injected on day 2 and day 3 between test cycle 1 and cycle 2. The injection occurred about 40 minutes prior to cycle 2. Because for some response variables, practice effects were evident through all four days, we decided to use only the day 2 data to assess the main effects of atropine. Table 1 shows that for the atropine group, d' scores decreased systematically through test cycles 2 and 3, whereas for the placebo group they remained approximately constant. Hits declined in both the atropine and placebo conditions, but the decrease was greater in the atropine group. False alarms increased in both groups from cycle 1 to cycle 3, but the increase was greater in the atropine group. As expected, neither β nor reaction time show systematic effects of atropine. Two-way (drug x cycle) analyses of variance for the day 2 data revealed significant drug x cycle interaction effects for d' ($F_{2,30}$= 3.5, p <.05) and for False Alarms ($F_{2,30}$ = 3.4, p <.05) but not for Hits ($F_{2,30}$ = 0.95, p <.40). There were no significant interaction effects for β or reaction time. Duncan's multiple range tests in the atropine group showed that the deficits in d' and Hits became significant only in cycle 3. For this reason we used only the cycle 1 and 3 data in further analyses of simple main effects. One-way analyses of variance within the atropine group, on day 2 (cycle 1-cycle 3) revealed significant effects for Hits ($F_{1,15}$= 9.1, p <.01), False Alarms ($F_{1,15}$ = 8.1, p <.02) and d' ($F_{1,15}$= 11.4, p <.01. Similar analyses of simple main effects in the placebo group revealed no significant effects of cycle. Figure 2 illustrates the effects of atropine on d' for both day 2 and day 3 (cycle 1-cycle 3).

These results support the hypothesis that atropine, like sleep loss, impairs perceptual functions associated with signal recognition (d') but does not alter response decision strategies indexed by the signal detection statistic, β.

A.1.c Effects of Atropine and Sleep Deprivation Combined

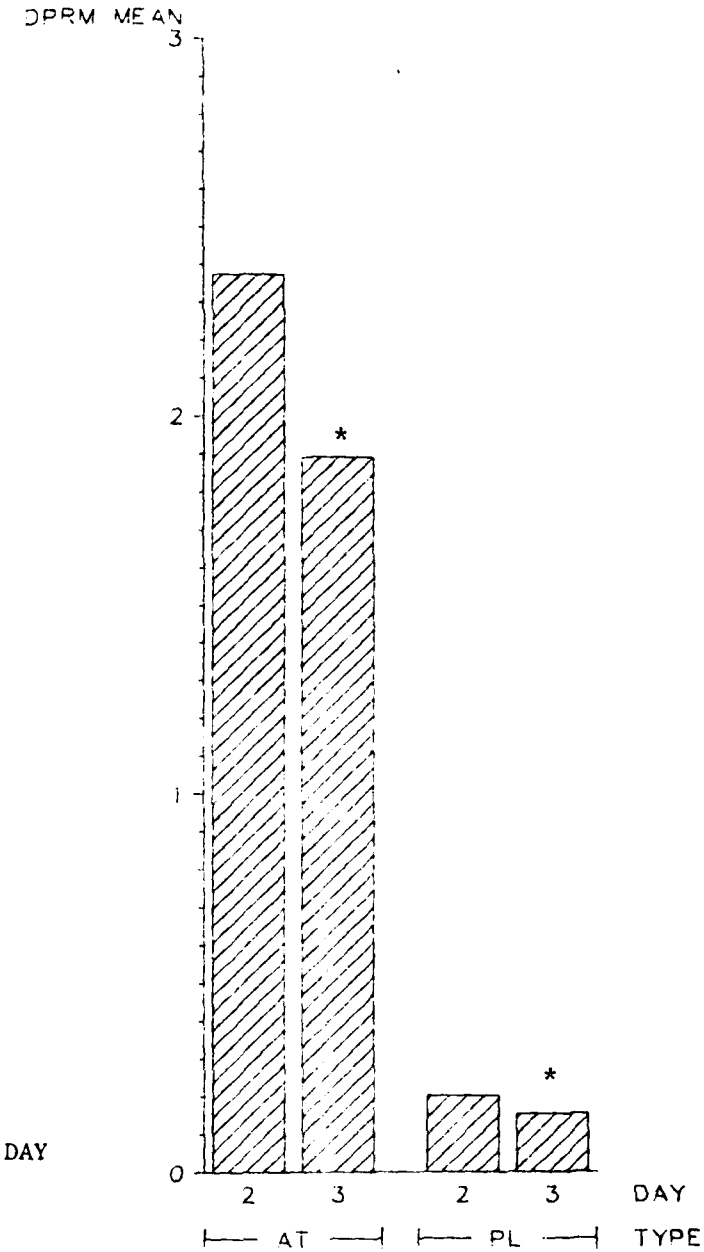
On day 3 all subjects had been sleep deprived and half the group received atropine. As seen in Table 1, the signal detection statistics show evidence of increasing impairment over test cycles on day 3 in the atropine group but not in the placebo group. Two-way (drug x cycle) analyses of variance on day 3 revealed significant drug x cycle interaction effects for d' ($F_{2,30}$ = 9.7, p <001), Hits ($F_{2,30}$= 4.8, p <.02) and False Alarms ($F_{2,30}$= 5.8, p <.01).

FIGURE 1
Aircraft Signal Detection (d')
(Effect of Sleep Deprivation)



* SLEEP DEPRIVATION DAY

FIGURE 2
Aircraft Signal Detection (d')
(Effects of Atropine)
(Cycle 1 - Cycle 3)



* SLEEP DEPRIVATION DAY

There were no significant interaction effects involving β or reaction time. Analyses of simple main effects using Duncan's multiple range test showed that the atropine-related deficits in the signal detection statistics reached statistical significance only in test cycle 3. There were no effects of cycle on reaction time or β.

In Figure 2, the average cycle 1-cycle 3 difference scores for the atropine condition are actually smaller on day 3 (sleep deprivation) than on day 2. This may be due to a floor effect for these scores. Performance in cycle 1 on day 3 was already impaired by a night of sleep deprivation. A two-way (drug x day) analysis of variance on the difference scores (cycle 1-cycle 3) found no significant drug x day interaction effects either for d' or for Hits.

A.2 Auditory Vigilance

A night of sleep deprivation and/or a 2mg dose of atropine each resulted in decreased d' scores on the Aircraft Signal Detection Task, with no systematic changes in the so-called "caution" statistic, β. These findings are consistent with the hypothesis that both atropine and sleep loss specifically impair perceptual sensitivity. However, the results do not inform us as to whether the atropine effects on aircraft detection are due primarily to peripheral impairment of visual acuity or to impairment of more central perceptual functions. It is well known that systemically administered atropine in doses of 2mg or more can cause both increased pupil size and paresis of accommodation (Headley, 1982). Our own data from Year 1 of this contract confirm the dose effects of atropine on pupil diameter. However, Baker and colleagues (1983), employing an atropine dose of 2mg per 70 kg body weight, found no effect of the drug on visual acuity for distant targets, three meters from the eye, nor was there impairment of performance on a visual search task where the display screen was 70cm from the eye. Since our display screen for the aircraft detection task is about 1 meter from the subject, we suspect that our atropine effects were due to central rather than peripheral effects.

The auditory vigilance task was included in the battery as a partial check on the notion that atropine effects on visual signal detection were due to impairment of central perceptual functions. Note, however, that this is not a strong test of the hypothesis. Thus, although a finding that atropine impairs auditory signal detection would be consistent with the hypothesis of central mediation, it is possible that atropine also alters peripheral auditory functions. Regardless of interpretation of the data, however, it is important to learn whether atropine at 2mg does impair auditory signal detection, and whether the effects of atropine interact with those of sleep deprivation.

Recall that the stimuli for the auditory vigilance task are a randomly ordered series of "pings" composed of 5 different pitches, the lowest of which is the target ping. The interstimulus interval is 2 seconds with 48 target pings per 7.5 minute-block and 4 blocks per session. The subject monitors the stimuli with eyes closed and is instructed to press a button as quickly as possible to each occurrence of the target ping. The response variables are the signal detection statistics, d' and β , percent hits and false alarms and

reaction time. Since the task lasts about 45 minutes, it was scheduled for only 2 performance cycles, one before and one about 3 hours after the drug dose.

Table 2 displays means and standard deviations for the auditory vigilance task. The 4 columns under each day represent trial blocks. Scores in the top half of the table are from the atropine subjects and placebo scores are shown in the second half.

A.2.a Effects of Sleep Deprivation on Auditory Vigilance

Perusing the means for cycle 1 in Table 2 (both atropine and placebo), one finds the same trends for the auditory vigilance task as were observed in the aircraft signal detection task. That is, compared to scores on day 2 and day 4, those on day 3 (sleep deprivation) show deficit. The signal detection statistics d' and Hits decrease on day 3 while False Alarms increase. The "caution" statistic, β, shows no systematic change on day 3. In the placebo group but not in the atropine group, mean reaction time does appear to increase on day 3.

To assess the effects of sleep deprivation on auditory vigilance performance, cycle 1 scores on day 3 were compared with those for day 2 + day 4, averaged. A 2(day) x 4(block) analysis of variance on each response variable revealed significant sleep loss effects on d' ($F_{1,18}$= 42.8, $p < .001$), Hits ($F_{1,18}$ = 46.7, $p < .001$) and False Alarms ($F_{1,18}$ = 21.1, $p < .001$). Sleep loss had no significant effect on reaction time or on the "caution" statistic, β.

Time on task (block) had no significant effects on d', False Alarms or Reaction Time but Hits decreased significantly ($F_{3,17}$ = 5.0, $p < .05$) and β increased ($F_{3,17}$ = 5.2, $p < .05$) over blocks, the largest changes occurring between blocks 1 and 2. Surprisingly, there were no significant sleep loss x blocks interaction effects on any of the response variables. The effects of sleep deprivation and time-on-task are usually hyperadditive. Figure 3 illustrates the main effect of sleep deprivation on d'. Note the decline in performance on day 3.

A.2.b Effects of Atropine on Auditory Vigilance

As can be seen in Table 2, vigilance performance tends to decline in cycle 2, after the atropine dose on day 2. However, a 2(drug) x 4(blocks) analysis of variance on the difference scores (cycle 1-cycle 2) for day 2 found no significant effects of either atropine or time-on-task on any of the response variables. A similar analysis of drug effects on the day 3 scores did reveal significant atropine effects on d' ($F_{1,18}$= 5.9, $p < .05$) and Hits ($F_{1,18}$ = 4.8, $p < .05$). There were no significant drug effects on the other response variables.

These results suggest that atropine effects on auditory vigilance are observed only after performance has already been degraded as in the sleep deprived state. They imply a hyperadditive interaction between the effects of atropine and sleep loss. However, the day x drug interaction effect was not statistically significant for any of the response variables.

Table 2a

Auditory Vigilance Task

GROUP

Atropine

DAYS

			1				2				3				4			
	Blocks		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Cycle	d'	$\bar{X}$	4.8	5.2	5.2	5.6	7.5	5.9	6.2	5.4	4.5	2.9	3.3	2.5	5.1	4.9	4.7	5.8
		S	2.9	2.9	2.8	2.8	2.8	2.9	3.3	3.6	2.0	1.2	3.1	1.0	2.0	1.9	1.7	1.0
	H	$\bar{X}$	89	92	85	95	95	91	85	85	82	66	62	66	94	84	85	83
		S	11	14	15	11	8	17	23	21	23	10	22	19	5	14	13	9
1	FA	$\bar{X}$	2.8	2.9	2.1	3.8	0.7	2.0	2.6	3.6	2.9	3.3	3.5	4.0	0.9	0.6	0.7	0.6
		S	5	7	5	8	2	4	6	9	5	6	6	6	1	1	1	1
	$\bar{e}$	$\bar{X}$	2.6	3.9	4.0	4.1	3.0	3.0	3.3	3.3	3.3	4.5	3.9	4.4	3.8	4.7	4.0	5.0
		S	2.2	1.9	1.8	1.5	2.0	2.1	2.1	2.1	1.9	1.3	1.8	1.5	1.9	0.9	1.9	0.1
	RT	$\bar{X}$	525	553	522	500	471	506	521	518	489	498	505	535	512	549	557	561
		S	94	88	80	82	107	114	108	96	88	93	101	102	116	102	114	70
	d'	$\bar{X}$	4.0	4.8	4.2	4.4	3.9	4.3	4.1	4.4	2.8	2.4	2.2	2.7	4.6	4.2	5.0	4.0
		S	1.9	2.4	2.3	2.2	1.7	3.1	2.8	2.8	0.6	0.8	0.9	1.5	2.0	2.1	2.8	1.8
	H	$\bar{X}$	90	89	87	76	85	80	80	80	74	65	59	59	92	82	85	83
		S	13	14	11	11	17	20	17	13	16	17	18	10	9	17	13	15
2	FA	$\bar{X}$	3.8	3.4	3.1	3.5	1.8	2.8	1.8	1.4	2.8	3.2	3.5	3.2	1.5	1.4	1.1	1.7
		S	6	7	6	7	2	4	3	2	3	4	4	5	1	2	1	2
	$\bar{e}$	$\bar{X}$	2.4	3.1	3.4	3.7	4.0	3.7	4.1	4.2	4.2	4.4	4.5	4.5	3.0	3.9	4.3	4.3
		S	2.0	2.1	2.0	2.2	1.9	1.6	1.6	1.6	1.4	1.2	1.2	1.2	1.8	1.9	1.5	1.1
	RT	$\bar{X}$	476	459	457	479	507	481	491	505	505	556	530	507	519	498	517	525
		S	87	125	110	76	94	121	83	90	84	51	76	61	113	101	99	111

Table 2b

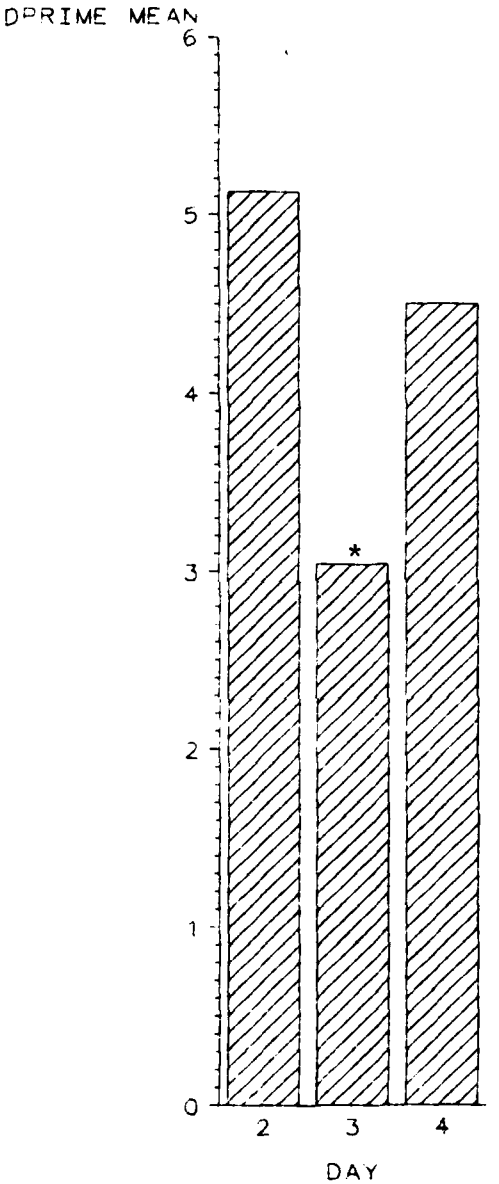
Auditory Vigilance Task

GROUP

Placebo

			DAYS															
			1				2				3				4			
Blocks			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Cycle	d'	$\bar{X}$	4.0	3.3	3.5	3.3	5.1	3.8	4.6	3.9	2.0	1.9	2.1	2.2	3.3	3.2	3.3	3.9
		S	2.9	2.0	2.3	2.8	4.1	3.2	3.7	3.2	1.0	1.7	1.6	1.7	2.3	2.5	2.4	3.1
	H	$\bar{X}$	86	75	70	73	84	76	78	75	60	49	55	55	79	71	74	79
		S	13	17	20	17	18	23	28	24	23	23	20	17	13	21	22	21
1	FA	$\bar{X}$	6.0	4.8	4.5	4.6	5.8	4.0	3.5	4.2	7.2	8.3	5.8	6.5	7.8	7.0	5.9	6.3
		S	9.3	6.3	4.7	5.0	6.3	4.9	3.7	4.3	7.0	8.5	5.2	8.4	9.5	10.2	7.0	8.3
	c	$\bar{X}$	2.3	3.8	3.7	3.3	1.6	3.4	2.6	3.2	3.2	3.2	3.4	3.8	3.6	3.7	3.5	3.0
		S	1.8	1.6	1.4	1.5	0.9	1.7	1.4	1.6	1.6	1.8	1.4	1.6	1.8	1.8	1.6	1.8
	RT	$\bar{X}$	521	513	521	520	489	503	523	500	521	549	519	523	491	492	487	496
		S	62	64	69	65	64	47	75	89	68	36	80	71	72	93	99	95
	d'	$\bar{X}$	3.2	3.6	3.4	3.2	4.4	3.0	3.9	3.7	2.0	2.0	2.0	1.9	3.3	3.0	2.9	3.0
		S	1.8	2.3	1.1	1.8	3.1	2.0	2.5	3.2	0.9	1.6	1.2	0.8	2.1	2.7	1.7	1.7
	H	$\bar{X}$	84	75	68	71	84	74	78	74	62	53	49	56	79	70	72	76
		S	14	15	20	18	17	19	19	24	20	13	12	14	19	30	24	18
2	FA	$\bar{X}$	7.5	4.9	4.7	5.8	5.8	2.6	4.7	4.8	8.3	7.5	6.3	6.6	10.6	8.9	6.2	6.1
		S	9.5	6.1	4.9	4.3	9.5	5.4	7.7	5.0	11.1	7.0	5.7	6.5	16.0	10.7	8.3	8.6
	c	$\bar{X}$	2.5	3.8	3.5	3.8	3.1	2.1	4.1	2.9	3.4	3.3	3.5	3.5	3.5	2.9	3.4	3.4
		S	1.7	1.5	1.6	1.3	1.9	1.4	1.4	1.8	1.5	1.3	1.5	1.4	1.9	1.9	1.8	1.7
	RT	$\bar{X}$	500	540	528	547	475	486	500	501	529	527	540	507	467	501	487	482
		S	62	79	75	98	84	111	105	97	78	111	74	84	111	115	100	106

Figure 3
Auditory Vigilance (d')
Effect of Sleep Deprivation



* SLEEP DEPRIVATION DAY

Figure 4 shows mean d' scores (cycle 1-cycle 2) for days 2, 3 and 4 in the two drug conditions. Note that on days 2 and 3, the atropine group showed progressive impairment in cycle 2. On day 4, their performance improved in cycle 2. Day 2 performance by the placebo group also improved in cycle 2 and showed no systematic time-of-day effect on day 3.

To summarize, a night without sleep caused systematic impairment of auditory signal detection performance. The decline in Hits and increase in False Alarms were due to impairment of perceptual sensitivity (d') rather than to a change in response decision criteria (β).

Time on task (block) was associated with decreased Hits and increased β, but d' was not affected. This is a common finding in the literature on vigilance tasks (Broadbent, 1971). Sleep loss x time-on-task interaction effects are also commonly found (Sanders, 1983) but were not obtained in this study. The reasons for this negative result are not apparent in the data.

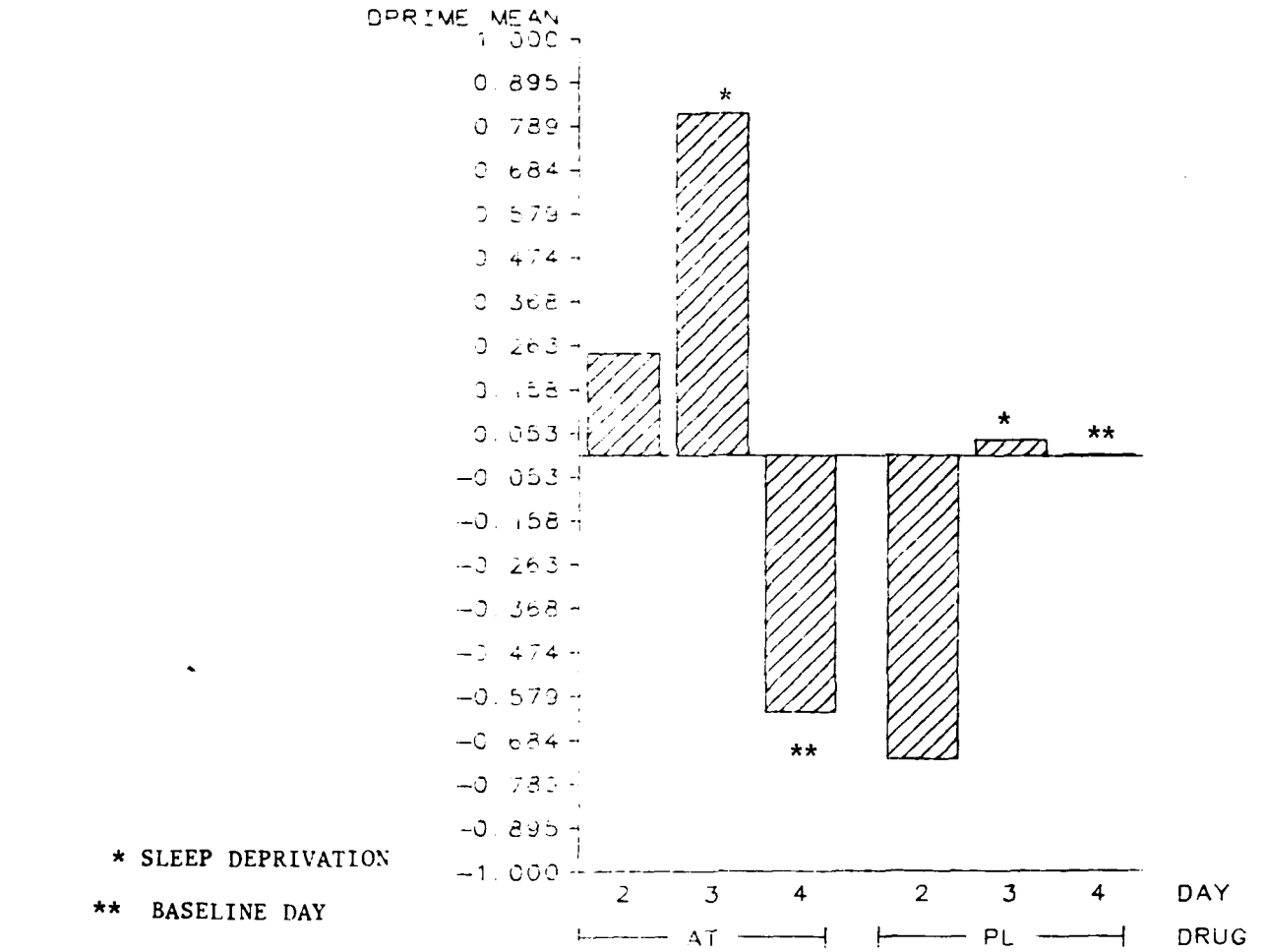
A 2mg dose of atropine caused small decreases in d' and in Hits in the auditory task which became statistically significant only in the sleep-deprived state. This trend toward a drug x sleep deprivation interaction effect was not quite statistically significant. We should note here that such trends will probably become significant as the sample sizes increase. The data reported above are based on only 10 subjects in each group.

A.3 Oddity Matching Task

This is a relatively high speed visual, 4-choice information processing task in which reaction time and motor time are the most important response measures. Recall that the stimuli consist of 4 dials arranged in a square, each containing a pointer, one of which is oriented in a different direction from the other 3. After detecting the odd pointer, the subject lifts his index finger from a center button (reaction time) as fast as possible and depresses a designated button located in one of 4 positions, also arranged in a square and oriented around the center button. Each response button is located 1cm from the center button. The movement from the center to the designated button provides a measure of ballistic motor time.

In an effort to specify the effects of atropine and sleep deprivation on the reaction process, we employed 3 task-related experimental variables: Signal Quality, Stimulus-Response (S-R) Compatibility and Time Uncertainty. In normal subjects, the effects of these variables on mean reaction time are additive (Sanders, 1983). Employing additive factor methods, advocates of serial-stage processing models infer that these task-related variables influence 3 different hypothetical stages in the reaction process. Thus, low signal quality selectively

Figure 4
Auditory Vigilance (d')
Effects of Atropine
(Cycle 1 - Cycle 2)



* SLEEP DEPRIVATION

** BASELINE DAY

Table 3

Oddity Matching Task

Cycle 1 Only

Day[a]	SQ[b]	SRC[c]	Cnty[d]	$\overline{RT}$[e]	RT_{sd}[f]	$\overline{MT}$[g]	PctE[h]
2	H	H	H	864	221	70	7
2	H	H	L	898	233	76	3
2	H	L	H	995	264	71	3
2	H	L	L	1067	289	82	4
2	L	H	H	1317	267	72	6
2	L	H	L	1424	294	78	3
2	L	L	H	1540	336	77	6
2	L	L	L	1636	340	84	4
3	H	H	H	887	279	83	6
3	H	H	L	947	302	88	5
3	H	L	H	1055	382	79	7
3	H	L	L	1107	322	88	4
3	L	H	H	1498	350	78	8
3	L	H	L	1563	363	85	8
3	L	L	H	1714	392	96	12
3	L	L	L	1743	413	93	7
4	H	H	H	811	208	70	4
4	H	H	L	871	227	72	3
4	H	L	H	1003	286	78	5
4	H	L	L	1026	268	78	3
4	L	H	H	1290	269	74	5
4	L	H	L	1370	255	76	3
4	L	L	H	1497	318	78	5
4	L	L	L	1566	309	78	3

a. Day 3, sleep deprived
b. SQ = Signal Quality (H = high quality)
c. SRC = Stimulus Response Compatibility
d. Cnty = Time Certainty
e. $\overline{RT}$ = Mean Reaction Time
f. $\overline{RT_{sd}}$ = Mean Standard Deviation, Reaction Time
g. $\overline{MT}$ = Mean Motor Time
h. PstE = Percent Error

slows performance in a stage associated with signal identification, low S-R compatibility slows a response choice stage and low time certainty impairs performance in a motor adjustment (motor preparation) stage.

A.3.a Effects of sleep deprivation on Oddity Matching

Table 3 contains mean cycle 1 scores on days 2, 3 and 4 for several response variables in each condition of each task-related experimental variable. Note that mean reaction time, the mean standard deviation of reaction time and motor time all tend to increase with sleep deprivation (Day 3). For analysis of sleep deprivation main effects, we computed the difference score $\frac{\text{Day 2 + Day 4}}{2}$ - Day 3 for each subject on each response variable in cycle 1 only. The mean differences were tested for statistical significance. Using the t-test for correlated means sleep loss caused significant increases in mean reaction time ($t = 5.0$, $p < .001$), mean standard deviation of reaction time ($t = 4.6$, $p < .001$) and mean motor time ($t = 2.1$, $p < .05$) but the increase in percent errors was not quite significant at the .05 level ($t = 1.9$, $p < .06$).

From the perspective of serial stage models of tbe reaction process, the response variable of greatest interest is mean reaction time. Previous work by others (e.g., Sanders, 1983) predict hyperadditive effects between sleep deprivation and 2 task-related variables, stimulus quality and time uncertainty on mean reaction time. The effects of sleep loss and SR compatibility should be additive. A 2(stimulus quality) x 2(SR compatibility) x 2(time uncertainty) analysis of variance was performed on the difference scores $(\frac{\text{D2 + D4}}{2} - \text{D3})$ for mean reaction time. Sleep deprivation did show hyperadditive interaction effects on mean RT with the task variable signal quality ($E_{1,29} = 23.6$, $p < 0001$). However, its effects were additive with both S-R compatibility and time uncertainty. Figure 5 illustrates the interaction between sleep deprivation and stimulus quality on mean reaction time. For the remaining response variables, the effects of each task variable were additive to those of sleep deprivation.

In summary, as anticipated from Sanders (1983), the effects of sleep deprivation on choice reaction time were considerably enhanced in the condition of low signal quality. However, the anticipated sleep loss x time uncertainty interaction effect was not found. Sleep deprivation also had significant main effects on reaction time variability and mean motor time but for these other response variables, there were no significant interaction effects involving the task-related experimental variables. From a theoretical perspective, the implication of the findings with reaction time is that one locus of sleep loss effects is an input processing stage involved in signal recognition, a stage that Sanders (1983) labeled "Feature Analysis."

The sleep loss x time uncertainty interaction effect found earlier by Sanders (1983) was consistent with the hypothesis that sleep deprivation also influences a motor adjustment stage in the reaction process. Our failure to find a similar interaction may be related to the fact that our time uncertainty variable had rather weak main effects on reaction time. In any case, the fact that sleep loss did cause slowing in ballistic motor speed is consistent with

Figure 5
Oddity Matching Task (RT)
(Day 2 + Day 4 - Day 3)
Interaction of Sleep Deprivation and Signal Quality

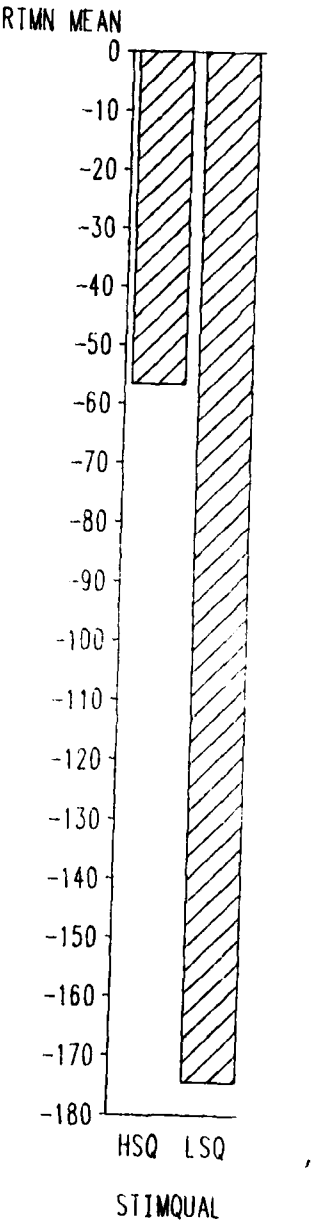


Table 4
Oddity Matching Task
Day 2
(Atropine and Placebo)

Atropine										Placebo									
Cycle	SQ	SRC	Cnty	RT	SD	RT_{sd}	SD	$\overline{MT}$	SD	Cycle	SQ	SRC	Cnty	RT	SD	RT_{sd}	SD	$\overline{MT}$	SD
1	H	H	H	851	145	201	60	66	21	1	H	H	H	897	182	240	83	73	31
1	H	H	L	860	186	212	83	79	24	1	H	H	L	935	185	253	109	73	25
1	H	L	H	971	212	26	[illegible]	68	24	1	H	L	H	1020	214	267	76	74	20
1	H	L	L	1028	189	264	95	87	42	1	H	L	L	1106	240	314	100	[illegible]	26
1	L	H	H	1335	181	266	85	68	21	1	L	H	H	1299	226	267	74	76	35
1	L	H	L	1428	212	300	100	84	32	1	L	H	L	1420	262	288	69	73	29
1	L	L	H	1540	231	306	143	74	25	1	L	L	H	1540	282	365	122	80	35
1	L	L	L	1667	251	357	149	91	26	1	L	L	L	1605	262	323	73	78	25
2	H	H	H	799	155	207	76	70	21	2	H	H	H	869	171	246	74	71	26
2	H	H	L	784	141	183	72	71	31	2	H	H	L	943	177	269	79	70	22
2	H	L	H	956	181	293	95	82	39	2	H	L	H	1067	250	292	119	71	28
2	H	L	L	976	151	278	69	85	39	2	H	L	L	1123	228	317	118	70	24
2	L	H	H	1354	308	290	87	77	34	2	L	H	H	1314	196	275	55	76	25
2	L	H	L	1381	238	280	69	79	41	2	L	H	L	1399	203	274	63	76	29
2	L	L	H	1582	253	357	70	91	45	2	L	L	H	1516	253	328	88	79	39
2	L	L	L	1620	293	359	85	82	37	2	L	L	L	1589	265	338	81	76	39
3	H	H	H	797	135	135	72	71	21	3	H	H	H	856	175	243	104	65	24
3	H	H	L	862	160	172	71	81	30	3	H	H	L	888	171	239	64	72	28
3	H	L	H	1002	248	204	126	79	25	3	H	L	H	1048	301	326	104	75	26
3	H	L	L	1009	218	219	149	87	31	3	H	L	L	1122	251	308	105	75	25
3	H	H	H	1395	235	182	104	81	25	3	L	H	H	1299	194	280	51	68	26
3	L	H	L	1498	294	194	87	82	31	3	L	H	L	1440	282	306	94	67	24
3	L	L	H	1689	362	215	158	84	34	3	L	L	H	1569	263	356	75	79	35
3	L	L	L	1708	320	215	129	84	35	3	L	L	L	1634	245	351	89	76	29

SQ = Signal Quality
SRC = S-R Compatibility
Cnty = Time Certainty
$\overline{RT}$ = Mean Reaction Time
RT_{sd} = Mean Standard Deviation
$\overline{MT}$ = Mean Motor Time

Table 5
Oddity Matching Task
Day 3
(Drug plus Sleep Deprivation)

				Atropine									Placebo					
Cycle	SQ	SRC	Cnty	RT	SD	RT_{sd}	SD	$\overline{MT}$	SD	Cycle	SQ	SRC	Cnty	RT	SD	RT_{sd}	SD	$\overline{MT}$	SD
1	H	H	H	851	158	245	102	86	41	1	H	H	H	924	173	257	86	80	30
1	H	H	L	911	192	305	224	98	46	1	H	H	L	983	216	298	142	78	26
1	H	L	H	983	371	350	201	76	47	1	H	L	H	1122	261	411	187	81	36
1	H	L	L	1043	255	260	91	95	51	1	H	L	L	1171	200	364	191	82	31
1	L	H	H	1479	327	344	145	81	41	1	L	H	H	1317	290	356	141	75	26
1	L	H	L	1541	327	389	241	96	42	1	L	H	L	1584	210	388	118	74	25
1	L	L	H	1675	337	342	173	91	48	1	L	L	H	1753	249	312	122	100	47
1	L	L	L	1693	273	349	137	96	46	1	L	L	L	1792	186	477	205	91	40
2	H	H	H	914	201	282	98	86	38	2	H	H	H	897	155	275	109	75	30
2	H	H	L	1058	305	447	180	83	29	2	H	H	L	961	206	329	183	76	28
2	H	L	H	1129	269	379	169	93	45	2	H	L	H	1117	241	357	110	76	28
2	H	L	L	1129	238	375	136	95	48	2	H	L	L	1159	222	369	204	75	25
2	L	H	H	1675	346	470	223	89	47	2	L	H	H	1514	212	355	135	80	34
2	L	H	L	1716	352	413	217	84	34	2	L	H	L	1617	249	410	168	79	41
2	L	L	H	1858	403	428	181	96	47	2	L	L	H	1709	237	410	229	81	44
2	L	L	L	1889	316	419	158	102	45	2	L	L	L	1761	222	396	115	75	41
3	H	H	H	958	275	362	197	86	18	3	H	H	H	944	171	185	154	73	44
3	H	H	L	1009	244	398	185	98	42	3	H	H	L	933	245	262	114	82	50
3	H	L	H	1182	324	438	264	105	49	3	H	L	H	1196	290	401	158	79	37
3	H	L	L	1254	349	489	364	96	42	3	H	L	L	1092	314	349	117	75	34
3	L	H	H	1650	344	479	280	96	35	3	L	H	H	1451	341	425	355	75	35
3	L	H	L	1719	342	483	232	107	43	3	L	H	L	1442	361	371	163	86	57
3	L	L	H	1947	324	472	144	111	58	3	L	L	H	1722	345	426	215	86	44
3	L	L	L	2000	303	464	121	119	55	3	L	L	L	1756	320	555	380	78	44

the notion that sleep deprivation impairs motor adjustment.

A.3.b Effects of Atropine on Oddity Matching

Tables 4 and 5 contain means and standard deviations of the atropine and placebo groups for each task cycle in each condition on day 2 (atropine alone) and day 3 (atropine plus sleep deprivation). Recall that task cycle 1 occurred prior to injection of atropine or placebo. From the perspective of a serial stage model of the reaction process, the response variable of greatest interest is again mean reaction time. For day 2 (Table 4), perusal of the RT scores of the atropine group reveals no marked overall drug effect. However, hyperadditive Drug x Signal Quality interaction trends can be seen, particularly in the cycle 3 data. Thus, for the atropine group, the effects of Signal Quality on reaction time increase from about 570 ms in cycle 1 to about 600 ms in cycle 2 and to approximately 660 ms in cycle 3 at about 4 hours post dose. No such time-of-day trend occurs in the placebo group. These data suggest that atropine did affect mean reaction time but only in the presence of low signal quality.

To examine these trends statistically, we first computed the cycle 1-cycle 3 difference score for each subject on each response variable, combining across levels of the task-related variables. T-tests for independent means were then used to compare the atropine with the placebo scores. Overall drug group differences on the response measures listed in Table 4 were not statistically significant for any response variable.

Employing the same cycle 1-cycle 3 difference scores, we then conducted a 2(Signal Quality) x 2(S-R Compatibility) x 2(Time Uncertainty) analysis of variance within the atropine group for each of the response variables in Table 4. A drug x task variable interaction effect would now appear as a significant main effect of the task variable. Signal Quality proved to have a significant effect on the mean reaction time difference score ($F_{1,14} = 7.2$, $p < .02$). There were no other significant main effect or interaction effects involving the remaining response variables or the other task-related experimental variables. A similar analysis on cycle 1-cycle 3 difference scores in the placebo group revealed no significant main effects or interactions for any response variable.

The scores in Table 5, obtained in the sleep deprived state (day 3) do suggest an atropine main effect on mean reaction time. Thus, the median of the mean reaction time scores increased from about 1200 ms in test cycle 1 to about 1400 ms in cycle 2 and to 1650 ms in cycle 3. In the placebo group, the corresponding median scores are about 1340, 1320 and 1270 ms for cycles 1, 2 and 3, respectively. Again, it appears that atropine does cause slowing of mean reaction time, but only when performance has been degraded by certain other conditions such as poor signal quality or sleep deprivation. These latter trends suggest a hyperadditive interaction between the effects of atropine and sleep deprivation. The trends in Table 5 also suggest that the drug x signal quality interaction effect on mean reaction time will again prove significant.

To analyze these effects, we first performed 2(Drug) x 2(Signal Quality) x 2(S-R Compatibility) x 2(Time Uncertainty) analyses of variance on the

cycle 1-cycle 3 difference scores for each response variable. The effect of atropine on mean reaction time was significant ($F_{1,28}$ = 13.5, p <.001), as was the drug x signal quality interaction effect ($F_{1,28}$= 10.1, p <.004). There were no significant main effects or interactions involving any task related variables on any of the other response variables listed in Table 5.

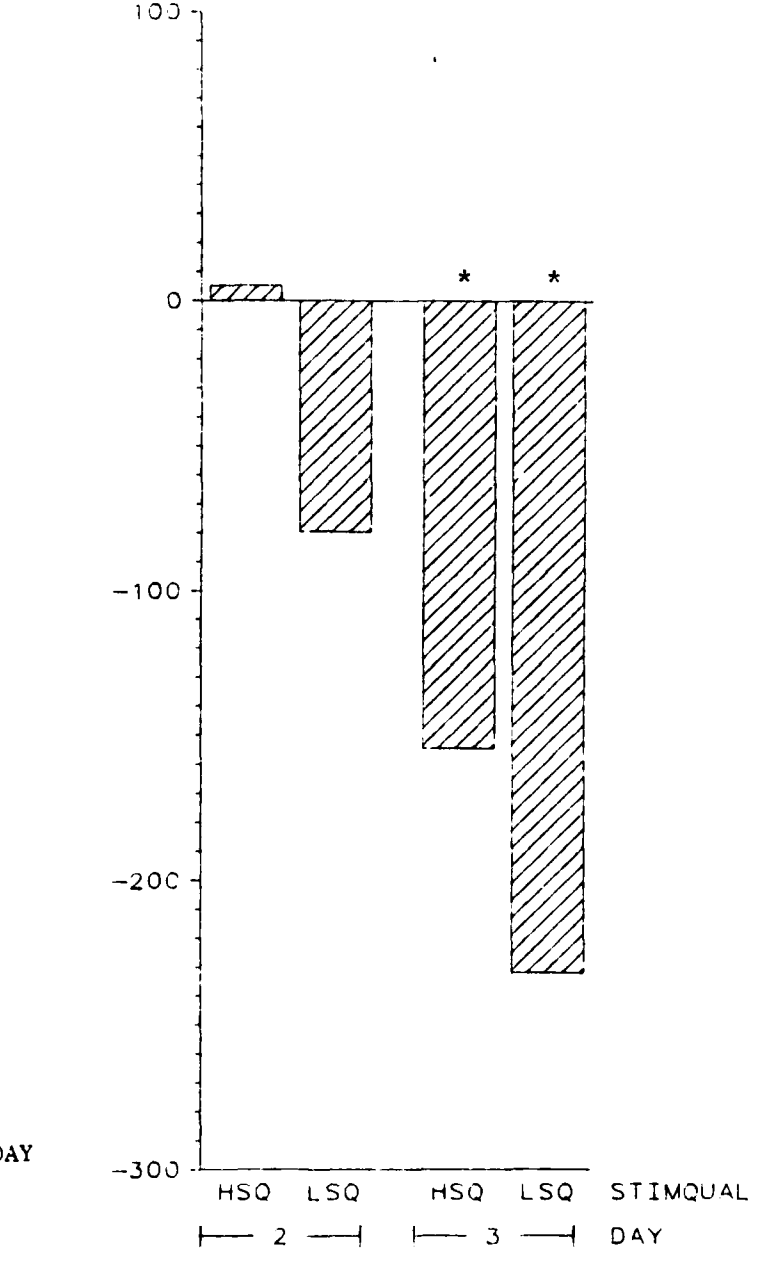
At this point our analyses have shown that both sleep deprivation and atropine effects interact hyperadditively with those of signal quality on mean reaction time in the Oddity Matching Task. Moreover, trends in the data suggest a similar Drug x Sleep Deprivation interaction effect. It will be interesting, therefore, to know whether there is a significant 3-way interaction among these variables.

Adding day to the analyses as a 5th experimental variable, we performed another set of analyses of variance on the cycle 1-cycle 3 difference scores for each response variable. For mean reaction time, the main effect of atropine was significant ($F_{1,28}$ = 10.4, p <.004) as were the drug x day ($F_{1,28}$ = 8.5, p <.007) and the drug x signal quality ($F_{1,28}$ = 6.7, p <.05) interaction effects. There was no trend toward a significant 3-way interaction between the effects of atropine, sleep deprivation and signal quality on mean reaction time (F <1.0). Figure 6 illustrates these findings for the atropine group. Note that since mean reaction time tends to increase after atropine, the cycle 1-cycle 3 difference scores tend to be negative. The 2-way interaction between atropine and signal quality can be seen on both day 2 and day 3, with atropine having no effect at all in the condition of good signal quality on day 2. On day 3, however, with performance already degraded by sleep deprivation, atropine slows reaction time by about 150 ms even when signal quality is good and by about 230 ms when signal quality is poor. Thus, Figure 6 illustrates the 2-way hyperadditive interaction effects between atropine and signal quality on the one hand and atropine and sleep deprivation on the other. The figure also illustrates the absence of any trend toward a 3-way interaction effect among the experimental variables.

B. Self Ratings

Mood assessment was done 6 times a day, twice before and 4 times after injection. After the atropine doses on days 2 and 3, there were significant increases in reported sleepiness, drunkenness, and dizziness. With atropine, subjects also reported that they felt less efficient, less able to attend, slowed, and less able to think. Some of these same items also showed significant effects of sleep deprivation. Thus, sleep deprived subjects reported that they felt less able to sustain attention and to think clearly. Surprisingly, there was no significant main effect of sleep loss on reported sleepiness, slowing or efficiency. For most of the atropine-sensitive items there were significant 3-way, day x drug x time-of-day interaction effects. Analyses of simple effects found evidence for drug x sleep deprivation interaction effects on Sleepiness (p <.04), Drunkenness (p <.04), Efficiency (p <.02), Ability to Think (p <.003) and on 2 other items, Dizziness and Discomfort. Insofar as these assessments reflect motivation and morale they show that the negative effects of atropine are significantly enhanced in the sleep deprived state.

Figure 6
Oddity Matching Task (RT)
Cycle 1 - Cycle 3
Effects of Drug, Sleep Deprivation and Signal Quality



* SLEEP DEPRIVATION DAY

C. Physiological Variables

C.1 Autonomic Measures

Table 6 contains mean scores on heart rate, systolic and diastolic blood pressure and pupil size. Cycle 1 measurements occurred prior to drug injection and the recordings labeled "Pre 2" took place about 30 minutes after injection. Comparing the cycle 1 scores for day 3 (sleep deprived) with those of the other days, it is clear that a night of sleeplessness had no systematic effects on any of the autonomic variables. However, as expected from our own previous work and that of many other investigators, atropine caused increases in heart rate and pupil size. In the atropine group, shown on the left half of Table 6, heart rate accelerated from about 65 BPM in cycle 1 to about 89 BPM following injection. At the end of testing (about 1745) mean heart rate was still about 8 to 10 BPM above the morning baseline. Note also that on both day 1 and day 4 (baseline) the atropine group had accelerated heart rates from middle to late afternoon. This same diurnal afternoon acceleration is seen on all 4 days in the placebo group. Taking account of this afternoon shift, it is clear that by late afternoon the atropine induced tachycardia had subsided almost to baseline levels. As expected from these trends, the effect of atropine on heart rate was highly significant ($F = 26.8$, $p < .001$), the diurnal effects in the placebo group were also highly significant ($F = 41.0$, $p < .001$), but the atropine effects were significantly greater than these baseline diurnal changes. For the 3-way interaction among drug, day and cycle, the $F = 18.4$, $p < .001$.

Following atropine injection on days 2 and 3 (left half of Table 6), pupil diameter had begun to increase at about 30 minutes post injection (Pre 2), reached peak diameter about 2 1/2 hours post injection, and remained considerably above baseline levels at the end of the afternoon. In the placebo group (right half of Table 6), there appear to be no systematic diurnal effects. For the 3-way, atropine x day x cycle interaction effect, $F = 8.5$, $p < .05$, and the Duncan's Multiple Range Test, performed within the atropine group, showed that all of the post-injection pupil diameters were significantly larger than those in the morning baseline.

Blood pressure has usually not been sensitive to 2mg atropine, at least in rested subjects. As expected, mean systolic blood pressure, Table 6, shows no trends either with atropine or for diurnal effects, and analysis of variance found no significant changes in systolic pressure either with sleep loss, atropine or recording cycle. However, the mean diastolic pressures shown in Table 6 do appear to increase following atropine injection on both day 2 and day 3. On day 2, mean diastolic pressure rises from 74 to 77 mm Hg at about 30 minutes, remains at 77 for at least 90 minutes (post-2) and then subsides to baseline levels. The same pattern is seen on day 3. No such trends occur in the placebo group. As anticipated from these trends, the day x cycle interaction effect proved statistically significant ($F = 13$, $p < .001$). Duncan's range tests within the atropine and placebo groups showed a significant increase in diastolic pressure following atropine injection which declined to baseline levels by mid afternoon. This significant change occurred on both

Table 6

Autonomic Variables

Atropine						Placebo					
Day	Cycle	HR	SBP	DBP	PD	Day	Cycle	HR	SBP	DBP	PD
1	1	63	129	71	30	1	1	59	128	72	31
1	Pre 2	63	132	74	34	1	Pre 2	56	127	73	31
1	Post 2	62	128	72	32	1	Post 2	57	127	76	32
1	Pre 3	66	133	70	35	1	Pre 3	67	132	72	33
1	Post 3	68	132	71	32	1	Post 3	68	132	72	32
2	1	65	132	74	31	2	1	6	128	73	31
2	Pre 2	89	132	77	35	2	Pre 2	59	127	73	33
2	Post 2	87	127	77	36	2	Post 2	59	126	75	34
2	Pre 3	78	130	72	42	2	Pre 3	71	130	74	33
2	Post 3	73	128	70	39	2	Post 3	6	130	72	34
3	1	66	132	69	33	3	1	6	131	73	31
3	Pre 2	88	132	79	38	3	Pre 2	59	131	75	31
3	Post 2	89	129	77	37	3	Post 2	6	130	75	33
3	Pre 3	75	132	74	43	3	Pre 3	64	131	74	33
3	Post 3	74	129	73	40	3	Post 3	6	132	74	31
4	1	65	129	71	34	4	1	6	129	73	30
4	Pre 2	64	127	71	36	4	Pre 2	6	126	71	32
4	Post 2	63	131	72	34	4	Post 2	6	129	74	31
4	Pre 3	70	137	69	35	4	Pre 3	67	133	73	32
4	Post 3	70	134	70	34	4	Post 3	6	132	74	31

HR = Heart Rate in beats/min
SBP = Systolic Blood Pressure, mmHg
DBP = Diastolic Blood Pressure
PD = Pupil Diameter (Horizontal) mm

Cycles	Time
1	1000
Pre 2	1200 following injection by about 30 minutes
Post 2	1400 following test cycle 2
Pre 3	1545 preceding test cycle 3
Post 4	1745 final recording

day 2 and day 3. Baker et al (1983), employing 10 male subjects, found similar trends in diastolic blood pressure following an i.m. dose of 2mg/70kg atropine, but the post-injection increase was not statistically significant.

C.2 Multiple Sleep Latency Test

Since subjects do complain of drowsiness and fatigue following atropine injection, it is of interest to know whether a direct measure of sleepiness (sleep tendency) is sensitive to atropine effects and whether atropine and sleep loss have hyperadditive effects on sleepiness. The multiple sleep latency test used here is a modification of the method described by Carskadon and Dement (1982). Using the EEG (and EOG where necessary), sleep onset latency defined as 1 minute of stage 1 was measured once before drug injection at about 0945 and twice following the 1130 drug injection at about 1345 and 1730.

Table 7 shows mean sleep latencies in the atropine and placebo conditions. The times of testing given above are referenced as a.m., noon and p.m. On day 1 (baseline) both of the treatment groups show declining sleep latencies (increasing sleepiness) through the day. On day 2, the decrease in sleep latency appears to be greater following atropine than following placebo. On day 3, as expected, subjects are quite sleepy at the morning run. Compared to placebo on day 3, atropine again seems to have increased sleepiness.

Analysis of variance on the scores from the placebo group revealed a significant effect of day ($F_{3,11} = 16.9$, $p < .001$), which represents the very systematic effect of sleep loss on day 3. There were no other significant effects in the placebo group. If the atropine-related changes in means seen in Table 7 reflect systematic increases in sleepiness, then we should find a significant 3-way, drug x day x time-of-day interaction effect and we do ($F = 6.0$, $p < .05$). For the atropine group on both day 2 and day 3, sleepiness increases after injection. There are no significant time-of-day trends in the placebo group.

These results are consistent with the self-report data previously summarized. Atropine, like sleep deprivation, causes increased sleepiness which can be registered as a reduction in sleep latency. Moreover, the analyses of simple main effects derived from the significant drug x day x time-of-day interaction strongly suggest hyperadditive effects of atropine and sleep loss on sleep tendency.

6. Discussion

The results from the performance tasks provide findings that are directly concerned with the loci of effects of atropine and sleep deprivation upon information processing. First, atropine and sleep deprivation impaired the recognition and selection of visual and auditory signals. In both the aircraft signal detection task and the auditory vigilance task, these effects were found on d', the index of perceptual sensitivity and not on β, the index of response criterion. Second, in the Oddity Matching Task with mean reaction

Multiple [illegible] Test

Day	[illegible]	SI*	Day	[illegible]	SI
1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
1	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
1	[illegible]	[illegible]	[illegible]	[illegible]	9.2
			[illegible]	[illegible]	8.6
2	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
2	[illegible]	[illegible]	[illegible]	[illegible]	7.5
			[illegible]	[illegible]	9.1
3	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
3	[illegible]	[illegible]	[illegible]	[illegible]	3.0
3	[illegible]	[illegible]	[illegible]	[illegible]	3.7
4	[illegible]	[illegible]	[illegible]	[illegible]	7.1
4	[illegible]	[illegible]	[illegible]	[illegible]	8.8
4	[illegible]	[illegible]	[illegible]	[illegible]	10.0

* SI = [illegible]

time as the response variable, patterns of additivity and interaction among atropine effects, sleep deprivation and the task-related experimental variables provided evidence that both atropine and sleep deprivation selectively influence the same stage in the reaction process. That is, each treatment had hyperadditive interaction effects with the task variable, signal quality and simple additive effects with the other 2 task variables, S-R compatibility and time uncertainty. The task variable signal quality is targeted on a hypothetical stage in the signal identification process that Sanders (1983) labeled feature extraction. Third, although both atropine and sleep deprivation appear to cause selective slowing in a signal processing stage, they may not influence the same functions within that stage. If atropine and sleep deprivation impaired the same processes within a stage, then one would expect to find a significant 3-way interaction involving signal quality. There was no trend toward such a 2nd-order interaction effect. Fourth, the effects of 2mg of atropine on cognitive performance are subtle and delayed. Whereas strong atropine effects were found on the autonomic variables, heart rate, pupil size and diastolic blood pressure at about 60 minutes post-injection, cognitive impairment was found only at 2 to 4 hours post-injection. Further, in both auditory monitoring and visual oddity matching significant atropine-related deficits were observed only after performance had been degraded either by low signal quality or by sleep loss. Note that these effects were quite specific in that atropine potency was not enhanced by low S-R compatibility or high time uncertainty. Fifth, although sleep deprivation effects did not interact with those of time uncertainty, sleep loss did cause slowing of motor speed. This finding seems consistent with Sanders' (1983) hypothesis that sleep loss also impairs a motor adjustment stage in the reaction process.

Taken together, the findings with atropine are consistent with Warburton's (1977) view that cholinergic blockade produces an impairment signal discrimination which, depending on task characteristics, may be seen either as loss of accuracy or slowing in response speed. In the signal detection tasks, the decrease in Hits and increase in False Alarms suggest that in the atropine state irrelevant or unattended stimuli cannot be filtered out in the normal fashion.

These results also suggest that the well-known effects of the cholinergic blockade and of sleep loss on recall and recognition may not be due to failure of consolidation or decay of the memory trace but instead to impairment of stimulus discrimination. Results recently reported by Dunne and Hartley (1985) in their studies of scopolamine effects on verbal memory are quite consistent with this hypothesis. They concluded that scopolamine modulates selective attention rather than memory consolidation processes and they invite greater consideration of attentional processes in any hypotheses concerning the effects of anticholinergic drugs on memory.

There is now considerable evidence that the effects of cholinergic antagonists on information processing are not due to peripheral cholinergic blockade. For example, Baker et al. found that atropine-induced pupillary dilation impaired visual acuity only for short-distance targets. Wesnes and Warburton (1984) showed that methscopolamine, a peripheral cholinergic blocker, did not cause deficit on a visual vigilance task. Dunne and Hartley (1985) found that

scopolamine impaired recall of words in dichotic listening tasks. Our finding that atropine impaired auditory vigilance is consistent with the general conclusion that the effects of atropine and scopolamine on information processing are centrally mediated.

What is the significance of these findings for performance of military jobs? First, any job in the field that requires high speed and accurate signal processing is likely to be vulnerable to atropine effects. Monitoring tasks such as radar, sonar, communications, or tracking tasks such as piloting, driving, and missile control are examples. Second, atropine-related impairment of accuracy and speed of signal processing will likely increase dramatically at dusk or in fog or in other conditions that impair signal quality. Finally, atropine impairment of information processing will likely be potentiated by sleep loss and in fact may be manifested only in the sleep-deprived state.

Atropine up to 2mg spares functions associated with response selection and motor control. Assuming that the selectivity of atropine effects holds for higher doses, soldiers dosed with atropine should be able to perform routine motor tasks about as well as in a normal state.

The effects of atropine on the autonomic variables are well documented in other laboratories and do not require interpretive discussion. It is perhaps important to note that except for pupil dilation these effects had returned approximately to baseline levels before we found any systematic effects on information processing.

The multiple sleep latency test which we introduced in Year 2 is of interest because it provides a direct measure of sleep tendency, or sleepiness. Sleep latencies were reduced both by atropine, confirming self-reports, and by sleep deprivation. Sleepiness, indexed by short sleep latencies, increased shortly after atropine injection and persisted to the final assessment of the afternoon. It is possible that sleepiness following atropine injection is responsible for the link between atropine and sleep deprivation in their effects on perceptual processing.

Bibliography

Baker, R., Adams, A., Jampolsky, A., Brown, B., Haegerstrom-Portnoy, G., & Jones, R. (1983). Effects of atropine on visual performance. Military Medicine, 148: 530-535.

Brown, K., & Warburton, D. M. (1971). Attenuation of stimulus sensitivity by scopolamine. Psychonomic Science, 22: 291-298.

Calloway, E. (1984). Human information-processing and some effects of methylphenidate, age, and scopolamine. Biological Psychiatry, 19(5): 649-662.

Carskadon, M. A., & Dement, W. C. (1982). The multiple sleep latency test: What does it measure? Sleep, 5: 567-572.

Dunne, M. P., & Hartley, L. R. (1985). The effects of scopolamine upon verbal memory: Evidence for an attentional hypothesis. Acta Psychologica, 58: 205-217.

Frowein, H. W. (1981). Selective effects of barbiturate and amphetamine on information processing and response execution. Acta Psychologica, 47: 105-115.

Frowein, H. W., Reitsma, D., & Aquarins, C. (1981). Effects of two counteracting stresses on the reaction process. In J. Long & Baddeley, A. (Eds.), Attention and Performance, IX. Hillsdale, N.J.: Lawrence Erlbaum Associates.

Headley, D. B. (1982). Effects of atropine sulphate and pralidoxine chloride on visual, physiological, performance, subjective and cognitive variables in man: A review. Military Medicine, Vol 147.

Rechtschaffen, A., & Kales, A. (1968). A Manual of Standardized Terminology: Techniques and Scoring System for Sleep Stages of Human Subjects. N.I.H. Publication No. 204, Bethesda, MD.

Sanders, A. F. (1983). Towards a model of stress and human performance. Acta Psychologica, 53: 61-97.

Sanders, A. F., Wijnen, J. L. C., & V. Arkel, A. E. (1982). An additive factor analysis of the effects of sleep loss on reaction processes. Acta Psychologica, 51: 41-59.

Steinberg, S. (1969). The discovery of processing stages: Extension of Donders' method. Acta Psychologica, 30, Attention and Performance II. Koster, W. G. (Ed.) North Holland Publishing, Amsterdam.

Vanderwolf, C., & Robinson, T. (1981). Reticulo-cortical activity and behavior: A critique of the arousal theory and a new synthesis in Brain and Behavioral Science, University Press, Cambridge.

Warburton, D. M. (1977). Stimulus selection and behavioral inhibition. In L. L. Iverson, S. D. Iverson, S. H. Snyder (Eds.), Handbook of Psychopharmacology, Vol 8: Drugs, Neurotransmitters and Behavior. New York: Plenum, 385-432.

Warburton, D. M. (1981). Neurochemical bases of behavior. British Medical Bulletin, 37, 121-125.

Warburton, D. M., & Brown, K. (1972). The facilitation of discrimination performance by physostigmine sulphate. Psychopharmacologia, 27, 275-284.

Wesnes, K., & WArburton, D. M. (1984). Effects of scopolamine and nicotine on human rapid information processing performance. Psychopharmacology, 82, 147-150.

Wilkinson, R. T. (1969). Sleep deprivation: Performance tests for partial and selective sleep deprivation. In Progress in Clinical Psychology. Grune and Stratton, Inc. USA.

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